

Prescription Opioids Dispensed to Patients with Cancer with Bone Metastasis: 2011–2017

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Disclosures of potential conflicts of interest may be found at the end of this article.

ABSTRACT

Opioid therapy is a first-line approach for moderate-to-severe pain associated with cancer with bone metastasis (CBM). The decade-long decline in opioid prescribing in the U.S. would not be expected to affect patients with CBM. We investigated trends in opioids dispensed to patients with CBM using data from a large commercial claims database. From 2011 quarter 2 to 2017 quarter 4, the percentage of patients with CBM prescribed at least 1 day of opioids in a quarter declined from 28.1% to 24.5% ($p < .001$) for privately insured patients aged

18–64 years and from 39.1% to 30.5% ($p < .001$) for Medicare Advantage (MA) patients aged 65 years or older. Among patients with at least 1 day of opioids in a quarter, the average morphine milligram equivalents dispensed declined by 37% and 11% ($p < .001$ for both) for privately insured and MA patients, respectively. Our findings raise concerns about potential unintended consequences related to population-level reduction in opioid prescribing. *The Oncologist* 2021;26:e1890–e1892

INTRODUCTION

Since 2011, the U.S. has seen a steady decline in opioid prescribing [1]. This change followed more than a decade of rising rates of opioid prescribing and prescription opioid misuse and overdose. Although the decline resulted from a national effort to reverse these opioid-related adverse outcomes, the changes in practices it reflects were not intended to affect populations for whom opioid therapy is clinically indicated [2, 3]. An important population are patients with cancer with bone metastasis (CBM). This population often has advanced illness and pain is a common complication. Specialists in palliative care and pain management consider opioid therapy to be the mainstay pain treatment [4] for this population.

A decline in opioids dispensed to patients with CBM, if seen, may represent unintended negative consequences and may lead to a rising rate of undertreated pain. Emerging concerns about this possibility (among CBM and other patients) led the Centers for Disease Control and Prevention (CDC) to formally clarify [5] that the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain [6] should not be applied to patients with pain associated with cancer, surgical procedures, or acute sickle cell crises. In this study, we

evaluated this possibility by assessing trends in opioids dispensed to adult patients with CBM during 2011–2017.

MATERIALS AND METHODS

We used data from the Health Care Cost Institute (HCCI) commercial insurance claims database, a national database covering approximately 50 million individuals each year. We conducted analyses separately for patients with CBM who were (a) privately insured and aged 18–64 or (b) Medicare Advantage enrollees and 65 years or older.

For each quarter (Q) from Q2 of 2011 to Q4 of 2017, patients were included if they were continuously enrolled and had at least one diagnosis of CBM in a calendar quarter. (Q1 of 2011 was not included because we did not observe opioid prescriptions dispensed in late 2010, which may be used in early 2011.) The maximum number of diagnostic codes in the HCCI data increased from 3 to 25 at the International Classification of Diseases, Ninth Revision (ICD-9) to International Classification of Diseases, Tenth Revision (ICD-10) transition in October 2015. We thus only used the first three diagnostic codes for all years of data when defining the samples.

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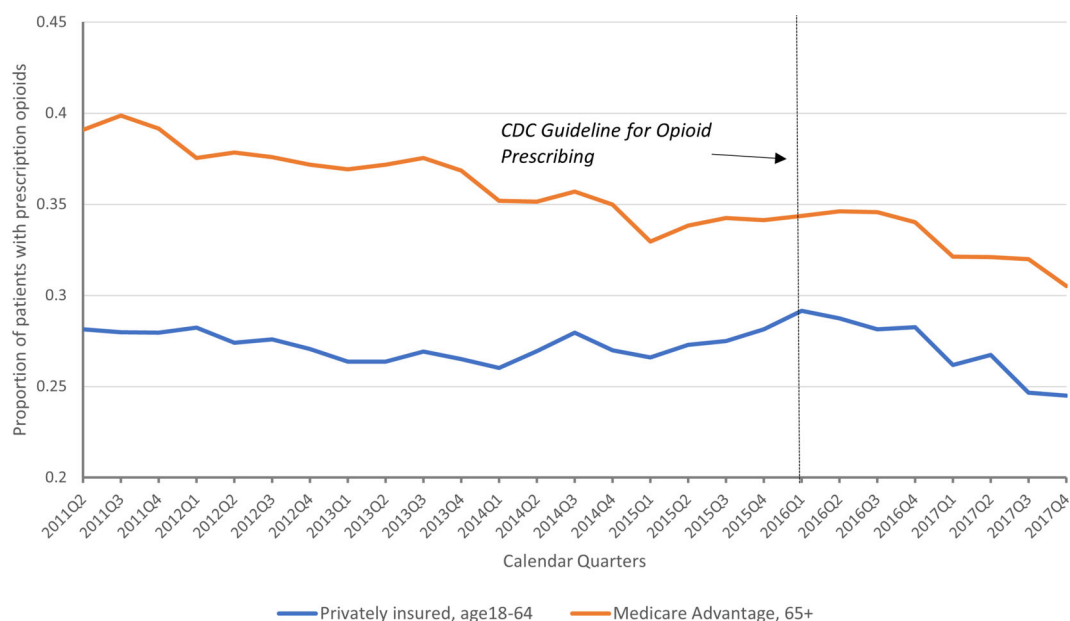


Figure 1. Percentage of patients with cancer with bone metastasis who had at least 1 day of prescription opioids in a calendar quarter: Q2 of 2011 to Q4 of 2017. Vertical dashed line represents Q1 of 2016, when the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain was published.

Abbreviations: CDC, Centers for Disease Control and Prevention; Q, quarter.

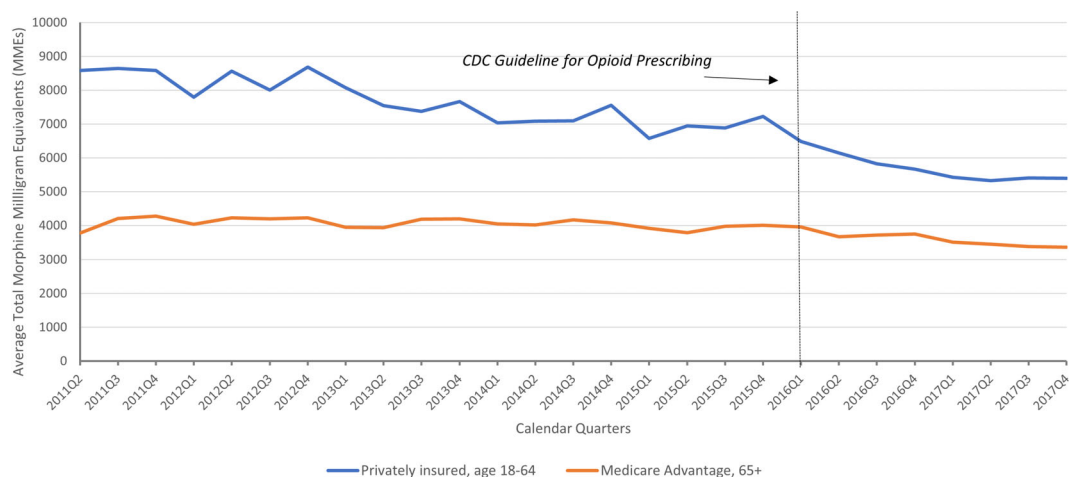


Figure 2. Average total MMEs dispensed to patients with cancer with bone metastasis with at least 1 day of prescription opioids in a quarter: Q2 of 2011 to Q4 of 2017. Vertical dashed line represents Q1 of 2016, when the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain was published.

Abbreviations: CDC, Centers for Disease Control and Prevention; MME, morphine milligram equivalent; Q, quarter.

Opioid prescriptions were identified from pharmacy claims using the National Drug Code. We constructed four outcome measures of prescription opioids dispensed to a patient in a quarter: (a) having at least 1 day of prescription opioids in a quarter and, conditional on having at least 1 day of opioids, (b) total morphine milligram equivalents (MMEs), (c) number of days covered by opioids (based on fill dates and days of supply of prescriptions), and (d) average daily MMEs (DMMEs). We derived quarterly means of the outcomes and their 95% confidence intervals (CIs). Cochran-Armitage test (for at least 1 day of opioids) and Spearman's rank-order test (for all continuous outcomes) were employed to test time trends.

All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC). The study protocol was approved by the Weill Cornell Medicine Institutional Review Board (protocol no. 1405015111).

RESULTS

Our samples included an average of 10,164 privately insured patients and 10,930 MA patients each quarter. Over the study period, the percentage of patients who had at least 1 day of opioids during a quarter declined for both patient populations, from 28.1% (95% CI, 27.3%–29.0%) to 24.5% (95% CI, 23.7%–25.3%) for privately insured patients with CBM (a 13% decline, $p < .001$ based on trend

test), and from 39.1% (95% CI, 37.8%–40.4%) to 30.5% (95% CI, 29.8%–31.2%) for MA patients (a 22% decline, $p < .001$) (Fig. 1).

Among patients with at least 1 day of opioids in a quarter, both populations saw declines in total MMEs received over the study period. For privately insured patients, average total MMEs declined from 8,581 (95% CI, 7,797–9,365) in 2011Q2 to 5,393 (95% CI, 5,004–5,781) in 2017Q4 (a 37% decline, $p < .001$). For MA patients, average MMEs declined from 3,777 (95% CI, 3,486–4,069) in 2011Q2 to 3,359 (95% CI, 3,203–3,516) in 2017Q4, an 11% decline ($p < .001$) (Fig. 2).

The average number of days covered by opioids during a quarter declined from 44.5 (95% CI, 43.3–45.7) to 40.1 (95% CI, 39.0–41.2) among privately insured patients (a 10% decline, $p < .001$) and from 39.1 (95% CI, 37.8–40.3) to 37.2 (95% CI, 36.5–37.9) among MA patients (a 5% decline, $p < .001$). Average DMMEs declined from 137.7 (95% CI, 127.5–147.9) to 101.0 (95% CI, 96.0–106.1) for privately insured patients (a 27% decline, $p < .001$), and from 72.8 (95% CI, 69.4–76.2) to 69.6 (95% CI, 67.7–71.6) for MA patients (a 4% decline, $p < .001$).

DISCUSSION

Opioids dispensed to adult patients with CBM and enrolled in private insurance or Medicare Advantage declined between 2011 and 2017. This finding was consistent with earlier studies of patients with cancer receiving palliative care [7] and patients with CBM [8]. Together, these findings raise concerns about possible unintended negative consequences for patients with CBM of policies and guidelines largely intended for populations with chronic noncancer pain. The declines observed among privately insured patients aged 18–64 accelerated in the second half of 2016, shortly after the publication of the CDC Guideline. The accelerated declines may also be partially attributable to recent policies addressing opioid prescribing, for example, state legislative limits on the duration or dosage of the initial opioid prescription to a patient or opioids for acute pain, which took effect in 26 states between March 2016 and December 2017 [9]. These laws largely exempt patients with active cancer or cancer treatment.

A principal limitation of our study is that claims data do not provide information regarding clinical indication or appropriateness of opioid prescriptions, or whether

patients prescribed opioids were being adequately monitored for risk of misuse and overdose. It is possible that the declines in opioids dispensed to patients with CBM represented reduced needs for opioids (e.g., as a result of new chemotherapies that are associated with lower pain or increased use of palliative radiation among patients with CBM) and/or reduction in inappropriate use or misuse of opioids in this population. Claims data did not allow us to assess the magnitude of these factors. Our study also did not assess implications of such declines for pain and quality-of-life–related outcomes for patients with CBM.

CONCLUSION

For patients with CBM, including privately insured patients aged 18–64 and Medicare Advantage patients aged 65 or older, the rate of opioid dispensing and the amount of opioids dispensed declined between 2011 and 2017. Future studies should assess the extent to which efforts to mitigate opioid-related adverse effects in populations without cancer may have unintentionally led to higher rates of undertreated cancer pain.

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DISCLOSURES

The authors indicated no financial relationships.

REFERENCES

- Guy GP Jr., Zhang K, Bohm MK et al. Vital signs: Changes in opioid prescribing in the United States, 2006–2015. *MMWR Morb Mortal Wkly Rep* 2017;66:697–704.
- Darnall BD. The national imperative to align practice and policy with the actual CDC opioid guideline. *Pain Med* 2020;21:229–231.
- Haffajee RL. Prescription drug monitoring programs—Friend or folly in addressing the opioid-overdose crisis? *N Engl J Med* 2019;381:699–701.
- Portenoy RK. Treatment of cancer pain. *Lancet* 2011;377:2236–2247.
- Dowell D, Haegerich T, Chou R. No shortcuts to safer opioid prescribing. *N Engl J Med* 2019;380:2285–2287.
- Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA* 2016;315:1624–1645.
- Haider A, Zhukovsky DS, Meng YC et al. Opioid prescription trends among patients with cancer referred to outpatient palliative care over a 6-year period. *J Oncol Pract* 2017;13:e972–e981.
- Shen C, Thornton JD, Newport K et al. Trends and patterns in the use of opioids among metastatic breast cancer patients. *Sci Rep* 2020;10:21698.
- Davis CS, Lieberman AJ. Laws limiting prescribing and dispensing of opioids in the United States, 1989–2019. *Addiction* 2021;116:1817–1827.